REMARKS

Claims 1-21, 26-30, 34, and 36-46 are pending. Acknowledgement of the priority claim to provisional application 60/094,096 filed July 24, 1998 is noted with appreciation. Currently, claim 34 stands rejected under 35 U.S.C. 102(e) as anticipated by Chee et al. (U.S. 5,856,104). All the pending claims stand rejected under 35 U.S.C. 112, first paragraph. Lastly, claims 13-21 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for not clarifying a relationship between DNA genotyping and determining FcαRI alleles. Independent claims 1, 13, 26, and 36 have been amended. Support for the amendments is found at page 33, lines 16-18, and as such it is submitted that no new matter has been added by way of this amendment.

Remarks Directed to Rejection of Claim 34 Under 35 U.S.C. 102(e)

Claim 34 recites the limitations of "reagents for identifying single nucleotide polymorphisms in a FcαRI together with instructions for the use thereof as a test to identify individual susceptibility to a disease." (Claim 34, lines 1-3).

Applicant submits that Chee et al. is incapable of performing the functions of pending claim 34. Specifically, Chee et al. recites at column 13, lines 46-47, that an inventive kit comprises "at least one alleles-specific oligonucleotide as described above." The 'above description' in Chee et al. only relates to glucose-6 phosphate dehydrogenase and as such, the oligonucleotides taught in Chee et al. are not in fact "reagents for identifying single nucleotide polymorphisms in a FcαRI genotype or phenotype." (Claim 34). Additionally, while Chee et al. recognizes that polymorphisms confer evolutionary competitive differences, different restriction fragment lengths, genetic diseases, etc. *See* column 1, line 11, column 2, line 10. Chee et al. is silent as to identifying a single nucleotide polymorphism that relates to

susceptibility to a disease. Instead, Chee et al. only recognizes polymorphisms that cause a genetic disease and this is not equivalent to susceptibility to the IgA related diseases that the present invention tests an individual with respect to their susceptibility thereto. Specifically, these diseases include the prototypical periodontal diseases, systemic lupus erythematosus, systemic vasculitis and IgA nephropathy.

On the basis of these remarks, it is submitted that claim 34 is not anticipated under 35 U.S.C. 102(e) by Chee et al. Withdrawal of the rejection of claim 34 as anticipated by Chee et al is solicited.

Remarks Directed to Rejection Under 35 U.S.C. §112, first paragraph

All of the pending claims are currently rejected as lacking enablement. Applicant submits that one skilled in the art upon a review of the written description of the invention would be able to practice the invention without undue experimentation for the reasons as detailed below. Applicant respectfully submits that the application of the factors is outlined in *Ex parte Forman,* and more commonly noted through their citation in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988) lacked an analysis as to whether each and every recited step of the claimed invention was enabled. With a finding of enablement for each and every element of the claimed invention, there is long standing case law that holds that the resulting invention is therefore enabled. Additionally, while Applicant believes that the In re Wands factors are satisfied by the instant specification (as detailed below) such a finding is not necessary to satisfy the enable requirements of Section 112. The Federal Circuit stated in *Amgen* that "it is not necessary that a court review all the *Wands* factors to find a disclosure enabling," Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1213 (Fed. Cir. 1991).

Turning to claim 1, the recited method step includes "identifying a FcαRI genotype of said cell." Example 3 which incorporates by reference references 12-14 specifically teaches the various FcαRI alleles (page 33, lines 16-18) as well as reciting in related examples how PCR. Figure 6 of the pending application is also relevant in detailing polymorphic cites within the receptor FcαRI. An alternative method of identifying a FcαRI genotype is provided in example 1 (page 37, line 19 - page 38, line 7). The technique of example 11 is further detailed in incorporated reference 63. As such, Applicant submits that there is sufficient teaching as to the identification of an FcαRI genotype for a cell in the instant specification.

The step of "quantifying IgA binding by said cell expressing said FcαRI genotype" (claim 1, line 4) is found in several places within the instant specification including examples 18-43 found at pages 40, line 13 - page 44, line 3. One skilled in the art would readily identify, (consistent with specification teaching at page 4, lines 10-13) that FcαRI is a native receptor for IgA and that binding occurs in native human neutrophils and monocytes. Applicant notes that the purification of IgA is described in detail in Example 18, as is the assay (Example 19), cell preparations (Example 20), and the culture for growing those cells (Example 21). A phagocytosis assay for quantifying IgA binding to cells is detailed in Example 23. Further, reference 147 incorporated by reference affords still another methodology for quantifying binding affinity of phenotypically different cells. Based on the specification teaching of Example 23 that notes that IgA or IgG are readily assayed by this method, I submit that one skilled in the art would readily appreciate the methods detailed in reference 147 are in fact readily applicable to the claimed invention, as indeed the case. Therefore, the Applicant submits there is adequate teaching within the specification to allow one skilled in the art to quantify IgA binding by a cell expressing a FcαRI genotype.

The third and final step of claim 1 involves repetition of the first two steps with a subject cell population that has a different genotype. In quantifying IgA binding differences between the two cell genotypes, standard experimental protocol well known to one skilled in the art dictates that quantification of the different genotypic cells is performed essentially identically so as to remove variables in the results potentially derived from procedural differences. As such, duplication of IgA binding quantification is submitted to require no further enablement. Correlation of IgA binding affinity by different genotypic cells with clinical disease manifestations for a given disease is as simple as charting laboratory results against the severity of clinical disease manifestation. The instant specification recognizes performing IgA binding assays for normal individuals in recognizing an individual falling statistically outside of the normal range therefore has an abnormal cellular susceptibility(e.g. page 14, lines 6-10). As such, Applicant believes that the third and final element of claim 1 is also enabled to allow one skilled in the art to practice the invention without undue experimentation.

The Examiner's concern that the specification lacks evidence as to the ability of FcαRI is contrary to the knowledge of one skilled in the art at the time the invention was made. In support of this position, the Examiner's attention is drawn to incorporated references that include references 43-50 of which, references 45-50 explicitly identify a role of IgA binding affinity in periodontal disease.

The final Office Action of October 9, 2003, at page 5, suggests that the specification is considered to lack enablement as to how to use the identification of a genotype once it has been discovered. Applicant notes that the specification at page 11, line 11 - page 12, line 2, identifies the value of genotypic information. Additionally, the final Office Action notes on page 5 that it is "unclear how the amount of bound IgA relates to the genotype of a cell.

Applicant respectfully submits that this point goes to the mechanism of efficacy and therefore isbeyond the requirements of enablement. However, Applicant submits that one skilled in the art from reading the specification and the prior art such as Chee et al. (referenced above) that single nucleotide polymorphisms are known to give rise to a variety of diseases based on the diminished binding ability of a receptor for a target. Chee et al. notes as examples single nucleotide polymorphisms and beta globulin and CFTR that are traced to cell genotype. Additionally, the background of the instant invention found on pages 6 and 7 notes significant data suggesting FcγRI that result in modified IgG binding relate to disease severity. (emphasis added). Based on this data and a desirability of determining if FcαRI genotype and IgA binding detailed at page 7, line 22 - page 8, line 4, the specification is submitted to suggest to one skilled in the art that a correlation exists. Applicant submits that at the time of the invention it was well known that the amount of IgA binding correlates with the magnitude of the immunological cascade. As such, Applicant respectfully submits that the position that there is no understanding of how IgA binding relates to cell genotype and therefore to disease susceptibility is contrary to the knowledge in the field which the invention pertains as of the date of invention.

The enablement of claim 1 as detailed above and the remarks relating thereto are believed to be equally applicable to the other pending claims.

In applying the *In Re Wands* factors with respect to the scope in the invention, the independent claims have been amended to specify the genotyping only of those cells that express FcαRI. As detailed above, these cells are specifically neutrophils and monocytes. These cell types were well known at the time of invention to bind IgA. From basic immunology, it follows that the ability to trigger the immune cascade system and elicit a rapid and strong immune response correlates directly to cellular binding of IgA. Thus,

Applicant submits that the variety of diseases associated with IgA-receptor mediated immune response detailed at page 19, lines 16-22 are representative of diseases where IgA binding and cellular susceptibility were well established at the date of invention.

As the above comments make clear that the practice of the various elemental steps of the claimed invention are enabled, Applicant would like to address the "how to use" prong of §112. The Courts have stated: "The enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engle Industries, Inc. v Lock Former Co.*, 945 F.2d 1526, USPQ2d 1300 (Fed. Cir. 1991).

As the making of the invention has been satisfied based on the above remarks, and the use of the claimed invention "as a diagnostic to identify high risk patients that warrant early and aggressive treatment," (specification page 11, lines 15-16) is believe to be met, therefore the enablement requirement is itself met. The implicit aspect of enablement to satisfy 35 U.S.C. §101 is likewise met based on this utility. Since it is irrelevant to objective enablement whether the required teaching is provided through broad terminology or a cluster of examples, a review of the specification as a whole indicates enablement of the claims in current form.

A review of the *In re Wands* factors in light of the amended claims indicates sufficient enablement.

(1) **The Quantity of Experimentation Necessary.**

There is virtually no experimentation needed to perform the various steps of the invention. The diseases to which single nucleotide polymorphism cell genotypes indicate the disease susceptibility are also detailed.

(2) **Amount of Direction or Guidance Presented.**

The specification teaches and extensively references the prior art to indicate that polymorphisms in FcαRI behave in a manner similar to that of FcγR receptors. The specification afford considerable data for FcγR. This teaching is not diminished because specific experimental data directed to FcαRI is not included within the specification. The "prophetic" correlation is stated in the application to exist, as claimed and is irrefuted by the Examiner. As such, enabling guidance and direction are in fact present within the specification.

(3) **The Presence or Absence of Working Examples.**

As detailed above, the specification examples provide specific recipes and methodologies for performing the claimed invention and in several instances, alternative methods for performing inventive steps, along with the advantages and disadvantages of each.

(4) **The Nature of the Invention.**

The claimed invention involves genotyping about specifically recited single nucleotide polymorphisms in a receptor of a known sequence in correlating cellular genotypes to susceptibility to IgA related diseases.

(5) **The State of the Prior Art.**

The state of the prior art with respect to cellular genotyping in clinical manifestations of IgA related diseases are both well developed as indicated by the more than 150 references

incorporated by reference into the pending application and available to provide still further enablement beyond that explicitly provided in the specification.

(6) **The Relative Skill of Those in the Art.**

The preparation of primers, culturing cells, genotyping those cells, assaying the cells for IgA binding, plotting those results relative to a clinical disease profile are commonplace skills in the art as evidenced by not only the specification itself, but the reliance on commercial kits and equipment. No where does the specification require the development of novel equipment, procedures of genotyping or assaying or any other skill beyond that commercially available.

(7) **The Predictability or Unpredictability of the Art.**

At the time of the invention, genotyping and assaying cells for IgA binding were considered to be routine tasks. Likewise, the ability to collect a cellular donor medical history and diagnose manifestations of IgA related disease were also routine tasks as of the date of invention.

(8) **The Breadth of the Claims.**

The breadth of the claims is broad with respect to disease correlation relating to FcαRI single nucleotide polymorphisms, but at the same time restrictive as to the receptor's allelic variations in correlation through IgA binding.

In total, application of the *In re Wands* enablement factors and the presently pending claims satisfy the enablement requirements.

In light of the above amendments and remarks, reconsideration and withdrawal of the rejection of all the pending claims under 35 U.S.C. §112, first paragraph, is solicited.

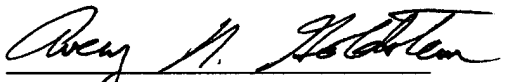
Remarks Directed to Rejection of Claims 13-21 Under 35 U.S.C. 112, second paragraph

Claims 13-21 are considered indefinite as not clarifying the relationship between DNA genotype and the determination of FcαRI alleles. In response to this rejection, independent claim 13 has been amended consistent with the final Office Action. In review of these amendments, withdrawal of the rejection of claim 13-21 under 35 U.S.C. 112, second paragraph, is solicited.

Summary

Claims 1-21, 26-30, 34 and 36-46 are the claims pending in this application. Entry of this amendment is requested. Reconsideration and allowance of the claims is also solicited.

Respectfully submitted,



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